

KINDLY AMEND THIS APPLICATION AS FOLLOWS:

In The Claims:

Amend claims 594, 710, 740, 871, 898, 1023, 1050, 1175, 1202, 1297, 1321, 1409, 1470, 1471, 1480, 1570, 1572, 1602, 1611, 1689, 1698, 1699, 1707 and 1718 as follows:

1 594. (Amended) The process according to claim 593, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide[,] and formaldehyde [and formamide].

2 ^{sub 6} ~~719~~ 719. (Amended) The process according to claim 569, wherein said modified or labeled nucleotides or nucleotide analogs are capable of being detected non-radioactively by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, [a calorimetric measurement,] a microscopic measurement and an electron density measurement.

3 746. (Amended) The process according to claim 745, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide[,] and formaldehyde [and formamide].

4 ^{sub 8} ~~871~~ 871. (Amended) The process according to claim 721, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, [a calorimetric measurement,] a microscopic measurement and an electron density measurement.

5 898. (Amended) The process according to claim 897, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide[,] and formaldehyde [and formamide].

sub 27 1023. (Amended) The process according to claim 873, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, [a calorimetric measurement,] a microscopic measurement and an electron density measurement.

U 1 1050. (Amended) The process according to claim 1049, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide[,] and formaldehyde [and formamide].

sub 35 1175. (Amended) The process according to claim 1025, wherein said one or more modified or labeled nucleotides or nucleotide analogs are capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, [a calorimetric measurement,] a microscopic measurement and an electron density measurement.

U 9 1202. (Amended) The process according to claim 1201, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide[,] and formaldehyde [and formamide].

sub 39 1297. (Amended) The process according to claim 1177, wherein said sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, [a calorimetric measurement,] a microscopic measurement and an electron density measurement.

U 11 1321. (Amended) The process according to claim 1320, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide[,] and formaldehyde [and formamide].

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1409. (Amended) The process according to claim 1298, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, [a calorimetric measurement,] a microscopic measurement and an electron density measurement.

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1470. (Amended) The process according to claim 1469, wherein said indirect detection is carried out by a means selected from the group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an enzyme, [a polynucleotide sequence capable of recognizing a signal-containing moiety,] a compound capable of binding to an insoluble phase, and a combination of any of the foregoing.

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✓ 51
1471. (Amended) The process according to claim 1411, wherein said nonradioactively detectable protein is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, [a calorimetric measurement,] a microscopic measurement and an electron density measurement.

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1480. (Amended) The process according to claim 1479, wherein said chemical coupling can be carried out by a chemical coupling means selected from the group consisting of carbodiimide[,] and formaldehyde [and formamide].

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1570. (Amended) The process according to any of claims 1473, 1474, 1475 or 1476, wherein said Sig detectable non-radioactive moiety is capable of being detected by a member selected from the group consisting of an enzymatic measurement, a fluorescent measurement, a phosphorescent measurement, a chemiluminescent measurement, [a calorimetric measurement,] a microscopic measurement and an electron density measurement.

1572. (Amended) The process according to claim 1473, 1474, 1475 or 1476,
wherein said one or more clones or DNA fragments or oligo- or polynucleotides
derived from clone or clones are derived from said particular chromosome or said
chromosome of interest or said chromosome in said interphase cell of interest.

1602. (Amended) The process according to claim 1601, wherein said chemical
coupling can be carried out by a chemical coupling means selected from the group
consisting of carbodiimide[,] and formaldehyde [and formamide].

1611. (Amended) The process according to claim 1582, wherein said labeled
[oligoor] oligo- or polynucleotide of interest prepared by said incorporating step
comprises at least one internal modified nucleotide.

1689. (Amended) The process according to claim 1582, wherein said labeled
[oligoor] oligo- or polynucleotide of interest is terminally ligated or attached to a
polypeptide.

1698. (Amended) The process according to claim 1697, wherein said detecting
step the indirectly detectable signal is provided by a member selected from the
group consisting of an antibody, an antigen, a hapten, a receptor, a ligand, an
enzyme[, a polynucleotide sequence capable of recognizing a signal-containing
moiety] and a combination of any of the foregoing.

1699. (Amended) The process according to claim 1582, wherein said Sig
detectable non-radioactive moiety is capable of being detected by a member
selected from the group consisting of an enzymatic measurement, a fluorescent
measurement, a phosphorescent measurement, a chemiluminescent measurement,
[a calorimetric measurement,] a microscopic measurement and an electron density
measurement.

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1707. (Amended) A process for determining whether the number of copies of a particular chromosome in a cell is normal or abnormal, the process comprising the steps of:

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contacting said cell under hybridizing conditions with one or more clones or DNA fragments, or oligo- or polynucleotides derived from said clone or clones, wherein said clones or fragments or oligo- or polynucleotides are capable of hybridizing specifically to a locus or loci of said particular chromosome or a portion thereof, wherein said clones or fragments or oligo- or polynucleotides comprise one or more detectable modified or labeled nucleotides or nucleotide analogs, which nucleotide analogs can be attached to or coupled to or incorporated into DNA or RNA, and wherein said modified or labeled nucleotides or nucleotide analogs are selected from the group consisting of:

(i) a nucleotide or nucleotide analog having the formula

PM - SM - BASE - Sig

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a pyrimidine, a purine, or a 7-deazapurine base moiety or an analog of any of the foregoing thereof, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to the SM, BASE is covalently attached to SM, and Sig is covalently attached to BASE at a position other than the C5 position when BASE is a pyrimidine moiety or an analog thereof, at a position other than the C8 position when BASE is a purine moiety or an analog thereof, and at a position other than the C7 position when BASE is a 7-deazapurine moiety or an analog thereof;

(ii) a nucleotide or nucleotide analog having the formula

Sig

PM - SM - BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to SM directly or through a linkage group; and

(iii) a nucleotide or nucleotide analog having the formula

Sig - PM - SM - BASE

wherein

PM is a phosphate moiety or phosphate analog,

SM is a sugar moiety or sugar analog,

BASE is a base moiety or base analog, and

Sig is a signaling moiety comprising a chelating compound or chelating component capable of providing a detectable radioactive signal, wherein PM is covalently attached to SM, BASE is covalently attached to SM, and Sig is covalently attached to PM directly or through a linkage group, to permit specific hybridization of said clone or clones or DNA fragments or [oligoor] oligo- or polynucleotides to the locus or loci of said particular chromosome;

detecting radioactively the signal generated by said specifically hybridized clone or clones or DNA fragments or oligo- or polynucleotides, and determining the number of copies of said particular chromosome; and

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Page 8 [Third Supplemental Amendment (Following Applicants'
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comparing said determined number of copies of said particular chromosome
with a number of copies of said particular chromosome determined for a normal cell
containing said particular chromosome, and determining whether the number of
copies of said particular chromosome in said cell is abnormal.

Sub 1718. (Amended) The process according to claim 1712, wherein said detecting
step is carried out by means of a member selected from the group consisting of
enzymatic measurement, a fluorescent measurement, a phosphorescent
measurement, a chemiluminescent measurement, [a calorimetric measurement,] a
microscopic measurement and an electron density measurement.
